



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-N-6084]

Type 2 Diabetes Mellitus: Evaluating the Safety of New Drugs for Improving Glycemic Control;
Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Type 2 Diabetes Mellitus: Evaluating the Safety of New Drugs for Improving Glycemic Control.” This draft guidance replaces the guidance for industry entitled “Diabetes Mellitus--Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes” and the draft guidance for industry “Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention,” both of which are being withdrawn. This draft guidance outlines the Agency’s current recommendations on the evaluation of safety for new drugs and biologics to improve glycemic control in patients with type 2 diabetes. Publication of this guidance is intended to provide clarity on the expectations for the development of drugs and biologics to improve glycemic control and to serve as a focus for commentary and feedback.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2019-N-6084 for “Type 2 Diabetes Mellitus: Evaluating the Safety of New Drugs for Improving Glycemic Control.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469,

September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Silvana Borges, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 3200, Silver Spring, MD 20993-0002, 301-796-0963.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Type 2 Diabetes Mellitus: Evaluating the Safety of New Drugs for Improving Glycemic Control.” This draft guidance replaces the guidance for industry entitled “Diabetes Mellitus--Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes,” published in

December 2008, and the draft guidance for industry “Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention,” published in February 2008, both of which are being withdrawn.

In response to questions and concerns about increased cardiovascular risk with certain antidiabetic therapies, FDA convened an advisory committee meeting in July 2008 to discuss the role of cardiovascular risk assessments for the safety evaluation of drugs and biologics developed for the treatment of type 2 diabetes. Based, in part, on comments expressed at that meeting, the Agency issued a guidance for industry in December 2008 outlining recommendations on the evaluation of cardiovascular risk for new antidiabetic therapies. That guidance stated that developers should demonstrate that new antidiabetic drugs and biologics would not result in an unacceptable increase in cardiovascular risk.

Since that time, FDA has reviewed the results of several cardiovascular outcome trials (CVOTs) conducted to meet the December 2008 guidance recommendations. None of the CVOTs to date have identified an increased risk of ischemic cardiovascular events; some of the CVOTs have instead demonstrated a reduced risk for cardiovascular events. In light of the CVOT results, FDA is revisiting the recommendations of the December 2008 guidance and is now proposing an updated approach to evaluating the safety of new drugs and biologics to improve glycemic control. In addition, FDA is withdrawing the February 2008 guidance because its recommendations for safety assessment have become outdated.

FDA is establishing this docket to solicit input from stakeholders on all aspects of these issues, including comments on specific questions posed in section II, Additional Issues for Consideration.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Type 2 Diabetes Mellitus: Evaluating the Safety of New Drugs for Improving Glycemic Control.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Additional Issues for Consideration

FDA is soliciting comments from stakeholders regarding the issues described in this notice and the draft guidance. In addition to any other aspects of the guidance that stakeholders may care to comment upon, FDA is interested in answers to the following questions/topics in particular:

A. Size of population and exposure to the investigational drug/biologic

1. Is it more important to emphasize the number of patients exposed or the amount of exposure (i.e., number of patient-years)? Or should there be expectations set for both parameters?
2. What would constitute a minimally acceptable database (either in number of patients, number of patient-years, or both) in terms of exposure to investigational drug/biologic at time of filing of the marketing application?

B. Demographic characteristics of the population

1. What are the important comorbid conditions to include?
2. What would be a minimally acceptable number of patients or number of patient-years to include for each important comorbid condition?

C. Necessary safety evaluations

1. Are there specific safety concerns for patients with type 2 diabetes that should be rigorously evaluated?
2. If there are specific safety concerns that should be rigorously evaluated, how should that assessment be conducted?
3. Is the adjudication of adverse events related to a specific safety concern a necessary part of the safety assessment? If so, should it be conducted by an independent, blinded adjudication committee or would other means of adjudication be adequate?

III. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved FDA collections of information. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collection of information in 21 CFR part 312 has been approved under OMB control number 0910-0014; the collection of information in 21 CFR part 314 has been approved under OMB control number 0910-0001; and the collection of information for clinical trial data monitoring committees has been approved under OMB control number 0910-0581.

IV. Electronic Access

Persons with access to the internet may obtain the draft guidance at either <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs> or <https://www.regulations.gov>.

Dated: March 5, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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